

lower than recommended, the incidence of VZV reactivation was low.

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Evaluation of Melphalan 1-Day Versus 2-Day Dosing in Patients with Multiple Myeloma Undergoing Autologous Stem Cell Transplantation

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Background: Multiple myeloma (MM) is the most common plasma cell disorder with an incidence of 4-5 new cases per 100,000 individuals per year. High dose chemotherapy with melphalan followed by autologous stem cell transplantation (SCT) is considered the standard of care. Melphalan 200 mg/m² is considered the gold standard conditioning regimen prior to autologous SCT. The Intergroupe Francophone du Myélome randomized trial confirmed that patients receiving melphalan 200 mg/m² displayed a better median overall survival as compared to patients treated with melphalan 140 mg/m² in combination with total body irradiation (65 vs. 45% survival at 45 months). Melphalan 200 mg/m² has been administered over 1-day or given over two consecutive days (100 mg/m² per day). Limited data exist on optimal schedule of dosing and to date, direct comparative efficacy analyses have not been conducted between 1-day versus 2-day melphalan administration. As of March 2012, the Blood and Marrow Transplantation Service at Moffitt Cancer Center changed the melphalan conditioning regimens from 2-day dosing (100 mg/m² per day) to 1-day dosing (200 mg/m² per day). An evaluation will be performed in order to determine if there is a difference in the effects on patients' transplant complications, engraftment, and response rates between the two groups.

The dose-limiting toxicity of melphalan is oral mucositis which is associated with prolonged hospitalization. Graziutti, et al found that higher melphalan doses and renal dysfunction (both reflecting increased melphalan exposure) were key pre-transplant risk factors for severe oral mucositis following autologous SCT; all doses were administered over 1-day. Parallel to this study, Palumbo, et al found a greater incidence of non-hematologic toxicities in patients who received higher doses of melphalan although this study evaluated melphalan 200 mg/m² versus 100 mg/m²; all doses were administered over 1-day. Along with toxicity profile, it is unknown whether administering melphalan over 1-day versus 2-days will affect response rates post-transplantation and progression-free survival of patients. We propose a retrospective comparison between patients who have received 1-day melphalan versus 2-day melphalan to evaluate these outcomes.

Study Design: A retrospective chart review of all patients with MM receiving high dose melphalan for autologous SCT from January 2010-October 2012 will be conducted.

Patient Population: Inclusion criteria:

- 1 All patients with primary diagnosis of MM undergoing autologous SCT
- 2 Conditioning regimen consisting of melphalan 200 mg/m²
- 3 18 years of age and older

Exclusion criteria:

- 1 Patients who received reduced dose melphalan, 140 mg/m², as conditioning regimen
- 2 For patients who received tandem autologous SCT, only the first SCT will be evaluated

Results: Preliminary results to be presented.

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Therapeutic Drug Monitoring (TDM) of Cyclosporine Using the Area Under the Curve in Children Undergoing Hematopoietic Stem Cell Transplant (HSCT)

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Introduction: The controversy surrounding cyclosporine TDM is still ongoing. In HSCT practice, the C0 method (or trough) is the one most commonly employed. At the CHU Sainte-Justine, the AUC method has been used for cyclosporine TDM in HSCT patients since October 2009. The aim of this study was to evaluate the correlation between cyclosporine levels (AUC or C0) with nephrotoxicity and GVHD in a pediatric population.

Methods: Forty-seven patients treated by IV cyclosporine for a first HSCT and having at least two AUCs were included in this retrospective study. Our protocol stipulates that a complete AUC (9 samples) must be done seven days after the beginning of the intravenous cyclosporine and partial AUCs (3 samples) once a week. All AUCs also include a C0. GVHD was defined as acute or chronic GVHD of any grade for the duration of the post-transplant follow-up. The patients were evaluated for the occurrence of nephrotoxicity according to the AKIN criteria.

Results: Median age of patients was 10.4 years (0.19-20.9). A total of 176 AUC samples were included (55 complete and 121 partial). Fourteen patients (30%) were diagnosed with GVHD and 23 (49%) with nephrotoxicity (AKIN stage 1, 2 or 3 at least one day for the duration of the IV cyclosporine).

All patients	Mean AUC _{24h} 21 days (ng.h/mL)			Mean C0 21 days (ng/mL)		
	12 581	Minimum 6531	Maximum 20168	202	Minimum 78	Maximum 430
With GVHD	12 561	p = 0.98		193	p = 0.64	
No GVHD	12 590			205		
With nephrotoxicity	12 345	p = 0.611		214	p = 0.360	
No nephrotoxicity	12 765			193		

Conclusion: No correlation was found between the cyclosporine levels (AUC or C0) and the occurrence of GVHD or nephrotoxicity. Many confounding factors can influence these issues and the small number of patients limits the extent of these findings.